Rare disease

Periampullary mass—a rare presentation of poorly differentiated neuroendocrine cancer of duodenum in a young adult: a case report and review of literature

Neha Singh, Hemanta K Nayak, Avishek Bagchi, Premashis Kar

Department of Medicine, Maulana Azad Medical College, New Delhi, New Delhi, India

Correspondence to Dr Hemanta K Nayak drhemantanayak@gmail.com

Summary

Poorly differentiated neuroendocrine tumour in the periampullary region of the duodenum is a rare entity. This entity usually present in old men. Here we report a periampullary poorly differentiated neuroendocrine cancer (PDEC) of duodenum presenting in a young man with subacute history of jaundice, abdominal pain, pancreatitis and constitutional symptoms. MRI localised the tumour and endoscopy-guided biopsy of the lesion proved the diagnosis. Although palliative surgery and chemotherapy were planned, the patient opted to leave against medical advice.

BACKGROUND

Poorly differentiated endocrine carcinomas (PDEC) of the gastrointestinal tract are rare tumours. A PDEC is defined as 'a malignant epithelial tumour composed of highly atypical, small-sized to intermediate-sized tumour cells growing in the form of large, ill-defined aggregate, often with necrosis and prominent angioinvasion and/or perineural invasion'.¹ In the older literature, these tumours have been variously described as high-grade neuroendocrine carcinomas, small-cell carcinomas, oat cell carcinomas, undifferentiated carcinomas or anaplastic carcinomas.

When applying the WHO criteria for PDEC, care should be taken to separate PDEC from mixed exocrine–endocrine tumours and exocrine tumours containing only *small number of endocrine cells*. Separation of PDEC from mixed exocrine–endocrine tumours is not always clear in the older literature. Owing to the rarity of gastrointestinal PDEC, comprehensive studies are still lacking on the epidemiology, clinical presentation, genetic alterations, histopathology, natural history and treatment of these tumours. Our knowledge of gastrointestinal PDEC is therefore limited and mainly based on a small series of patients and case reports.

CASE PRESENTATION

A 20-year-old male patient was admitted with 3-week history of postprandial colicky abdominal pain, recurrent vomiting and jaundice. He also complained of anorexia and weight loss. There was no history of alcohol abuse, gall stone disease, drugs intake or trauma to abdomen. Clinical examination revealed an afebrile, haemodynamically stable patient with significant positive findings of jaundice, tenderness over epigastrium and umbilical region.

INVESTIGATIONS

Laboratory reports revealed haemoglobin 105 gm/l (120–150), total leukocyte count 9100/mm³ (4000–11 000), differential leukocyte count polymorphs, 74; lymphocytes, 24; eosinophil, 2; random blood sugar, 5.77 mmol/l

(normal: 4.4–6.1); blood urea, 7.1 mmol/l (normal range 2.6–7.5 mmol/l); serum bilirubin, 6.5 mg/dl (direct 3.5 mg/dl, indirect 3.0 mg/dl); aspartate transaminase, 1021 U/l (normal range upto 40 IU/l); alanine transaminase, 106 IU/l (normal range upto 40 IU/l); serum alkaline phosphatase, 456 IU/l (normal range upto 170 IU/l); serum amylase, 757 IU/l (normal range upto 170 IU/l) and serum lipase 703 U/l (normal range upto 170 IU/l). Sodium and potassium levels were 132 and 4.8 mEq/l, respectively. Chest skiagram and ECG did not reveal any abnormality. Ultrasound of the abdomen revealed bulky pancreas with dilated common bile duct with heterogeneous mass near the head of the pancreas. His acute and chronic viral markers (*IgM anti-hepatitis A virus*, *IgM anti-hepatitis E virus*, *anti-hepatitis C virus* and *HbsAg by ELISA*) were negative, tumour markers (Carcino Embryonic Antigen - CEA, CA19–9, α fetoprotein) were also negative.

Since we suspected a periampullary tumour leading to obstructive jaundice and pancreatitis, an oesophagogastro-duodenoscopy and MRI abdomen were done. In the meantime the patient was managed conservatively. MRI abdomen (figure 1) revealed a soft tissue lesion in the first and second part of the duodenum causing stomach outlet obstruction and dilation and common bile duct dilation. Fat planes with head and neck of the pancreas were maintained (figure 2). There was no evidence of any lymph node or distant metastasis. Endoscopy showed globular swelling arriving from the duodenum, from which multiple biopsies were taken (figure 3). Duodenal biopsy revealed large atypical cells with scanty cytoplasm, increased N/C ratio and occasional nucleolus exhibiting a glandular pattern suggestive of poorly differentiated endocrine tumour (figure 4A,B). He developed ascites and an inguinal lymph node which started fungating and bleeding during his course of stay. Biopsy from inguinal lymphnodes suggestive of large atypical cells with scanty cytoplasm with areas of necrosis (figure 4C,D). The cells were reactive for epithelial membrane antigen (EMA). They were negative for CK, leukocyte

Figure 1 MRI of abdomen showing soft tissue lesion at the junction of first and second part of duodenum causing partial obstruction.

common antigen (LCA), HMB45, S-100, CK-20, placental-like alkaline phosphatase (PLAP), CD-30 and CD45RO, CA 19-9 and positive for neuron-specific enolase (NSE) suggestive of poorly differentiated neuroendocrine tumour of the duodenum (figure 4E,F).

DIFFERENTIAL DIAGNOSIS IF RELEVANT

- ▶ Acute pancreatitis
- ▶ Gastric outlet obstruction
- ▶ Abdominal lymphoma
- ▶ Abdominal tuberculosis

Figure 2 MRI of abdomen showing maintained fat planes between duodenal mass and pancreatic head.

Figure 3 Upper gastrointestinal endoscopy showing duodenal mass causing common bile duct and gastric outlet obstruction.

TREATMENT

- Conservative
- Palliative chemotherapy

OUTCOME AND FOLLOW-UP

The patient and his relatives refused for palliative surgical procedure and he was planned on palliative chemotherapy along with supportive care. Because of the financial constraints and poor outcome, the patient refused treatment and left against medical advice.

DISCUSSION

In the periampullary area, adenocarcinoma comprises more than 90% of all malignancies. Neuroendocrine tumours are rare in this area, and the majority of them are well-differentiated endocrine tumours (carcinoids).² Poorly differentiated endocrine carcinoma (small cell carcinoma and large cell neuroendocrine carcinoma) is extremely rare and only reported in case studies and small series.

Duodenal PDECs are primarily located in the ampulla of Vater⁽¹⁰⁾ and account for 2–3% of the ampullary tumours.³ The mean age of patients is 70 years with a male preponderance (M:F ratio 3: 1). Most patients present with jaundice and abdominal pain. Regional and/or distant metastases are usually present at diagnosis and a majority of patients die from tumour disease. The primary tumour present as a single lesion with a mean size of 2.5 cm. Half the tumours are associated with adenomas in the adjacent mucosa.⁴ The tumour mainly invaded the duodenum wall and pancreas aggressively (T3) but, on the contrary, lymph node metastasis was less commonly found. According to the WHO classification published in 2000, neuroendocrine neoplasms as compared with their pulmonary counterparts can be categorised into well-differentiated endocrine tumour (carcinoid), well-differentiated endocrine carcinoma (atypical carcinoid) and poorly differentiated endocrine carcinoma (small cell carcinoma and large cell neuroendocrine carcinoma). Metastases to lymph nodes are common.⁴ Our case a

20-year-old man with a soft tissue mass lesion in the first and second part of duodenum with features of obstructive jaundice initially localised with rapid dissemination to involve peritoneal cavity and inguinal lymphnodes during his hospital stay. There was no evidence of any coexistent adenoma or adenocarcinoma associated with this case.

In the literature reviewed, von Recklinghausen's disease or multiple endocrine neoplasia I (MEN I) is commonly associated with endocrine neoplasms of the duodenal papilla.⁵ Patients with carcinoids have a better prognosis than those with conventional adenocarcinoma. There was no evidence of any other endocrine malignancy or von Recklinghausen's disease in our case.⁵

Histopathology is required for the diagnosis. Routine histopathology and immunohistochemical staining for general neuroendocrine markers should be performed. Staining for specific hormones is usually negative. Additional neuroendocrine and non-neuroendocrine markers may be useful in the differential diagnosis. Cytology with fine needle aspiration is not recommended, but may be helpful. Histopathological features of ampullary PDEC include separation into two groups, large-cell and small-cell neuroendocrine carcinomas.⁶ A majority of tumours of both types stain positive for synaptophysin and chromogranin A. Herein we reported a large-cell variant of poorly differentiated neuroendocrine tumours of a young man which is strongly positive for NSE.

Imaging procedure should be determined from the clinical situation. CT, MRI, endoscopy with biopsy or endoscopic ultra sound (EUS), fludeoxyglucose positron emission tomography (FDG-PET). A minimal diagnostic procedure should include gastroscopy, CT or MRI.⁷ FDG-PET may be useful in the primary diagnosis and for staging. Somatostatin receptor scintigraphy (SRS) is not recommended but should be evaluated in the clinical setting. Surgical treatment that has been employed includes endoscopic resection, local excision and pancreaticoduodenal resection. Pancreatico-duodenal resection (Whipple's procedure) for larger tumours.

Systemic chemotherapy is indicated in inoperable disease, provided the patient has adequate organ function and performance status. Combined treatment with cisplatin/carboplatin and etoposide has been reported to induce remission in 55–80% of patients with response duration of 8–11 months.^{8–9} Chemotherapy may be considered in selected cases as adjuvant treatment; however, there are no data available to corroborate this opinion and studies are thus required. Somatostatin analogue treatment or interferon therapy is not recommended. The prognosis for patients with poorly differentiated endocrine carcinomas is generally poor. Patients with treated metastatic disease have an expected survival time of 6–12 months.¹⁰

Learning points

- Poorly differentiated duodenal neuroendocrine tumour presenting as periampullary tumour is a rare entity.
- Owing to the rarity of cases, additional studies of such tumours are required to understand their pathogenesis and management.
- Although PDEC usually present in old men, atypical presentation should be considered in young men presenting with non-alcoholic non gall stone pancreatitis.

Figure 4 (A and B) Duodenal biopsy revealed large atypical cells with scanty cytoplasm, increased N/C ratio and occasional nucleolus exhibiting a glandular pattern suggestive of poorly differentiated endocrine tumour (A, 10 $\times$ and B, 40 $\times$). (C and D) Biopsy from inguinal lymphnodes suggestive of large atypical cells with scanty cytoplasm with areas of necrosis (C, 10 $\times$ and D, 40 $\times$). (E and F) The cells were reactive for EMA. They were negative for CK, LCA, HMB45, S-100, CK-20, PLAP, CD-30 and CD45RO, CA 19-9 and positive for neuron-specific enolase suggestive of poorly differentiated neuroendocrine tumour of the duodenum.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Emory RE Jr**, Emory TS, Goellner JR, *et al.* Neuroendocrine ampullary tumors: spectrum of disease including the first report of a neuroendocrine carcinoma of non-small cell type. *Surgery* 1994;**115**:762–6.
2. **Bal A**, Joshi K, Vaiphei K, *et al.* Primary duodenal neoplasms: A retrospective clinico-pathological analysis. *World J Gastroenterology* 2007;**13**:1108–11.
3. **Sata N**, Tsukahara M, Koizumi M, *et al.* Primary small-cell neuroendocrine carcinoma of the duodenum: a case report and review of literature. *World J Surg Oncol* 2004;**2**:28.
4. **Nassar H**, Albores-Saavedra J, Klimstra DS. High-grade neuroendocrine carcinoma of the ampulla of Vater: a clinicopathologic and immunohistochemical analysis of 14 cases. *Am J Surg Pathol* 2005;**29**:588–94.
5. **Mayoral W**, Salcedo J, Al-Kawas F. Ampullary carcinoid tumor presenting as acute pancreatitis in a patient with von Recklinghausen's disease: case report and review of the literature. *Endoscopy* 2003;**35**:854–7.
6. **Sarker AB**, Hoshida Y, Akagi S, *et al.* An immunohistochemical and ultrastructural study of case of small-cell neuroendocrine carcinoma in the ampullary region of the duodenum. *Acta Pathol Jpn* 1992;**42**:529–35.
7. **Ricke J**, Klose KJ, Mignon M, *et al.* Standardisation of imaging in neuroendocrine tumors: results of a European Delphi process. *Eur J Radiol* 2001;**37**:8–17.
8. **Oberg K**, Ahlman H. Medical management of neuroendocrine gastrointestinal tumors. In Schwartz A, Gagner M, Pertsemides D, eds. *Endocrine surgery*. New York: Marcel Dekker, 2004: 685–96.
9. **Rougier P**, Mitry E. Chemotherapy in the treatment of neuroendocrine malignant tumors. *Digestion* 2000;**62**:73–8.
10. **Fjallskog ML**, Granberg DP, Welin SL, *et al.* Treatment with cisplatin and etoposide in patients with neuroendocrine tumors. *Cancer* 2001;**92**:1101–7.

This pdf has been created automatically from the final edited text and images.

Copyright 2012 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Singh N, Nayak HK, Bagchi A, Kar P. Periapillary mass—a rare presentation of poorly differentiated neuroendocrine cancer of duodenum in a young adult: a case report and review of literature. *BMJ Case Reports* 2012;10.1136/bcr-2012-007010, Published XXX

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow